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From: Roark, Jessica
Sent: Friday, January 10, 2003 12:20 PM
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Subject: OX-2

427198

STIC,

Please provide the following to

Jessica Roark,
9E12 mailbox, CM1

1. Gorczynski RM. Arch Immunol Ther Exp (Warsz). 2001;49(4):303-9. Review.
   PMID: 11726033 [PubMed - indexed for MEDLINE]

2. Clark DA, Semin Immunol. 2001 Aug;13(4):255-63. Review.
   PMID: 11437633 [PubMed - indexed for MEDLINE]

3. Nathan C, Nat Immunol. 2001 Jan;2(1):17-9. No abstract available.
   PMID: 11135572 [PubMed - indexed for MEDLINE]

Thanks!

Jessica H. Roark
CM1 8A03
Mailbox 9E12
Art Unit 1644
703 605-1209

9264788

WEST Search History

DATE: Friday, January 10, 2003

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DB=USPT,PGPB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=OR			
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L3	L2 and @PD<19971107	24	L3
L2	L1 and @RLAD<19971107	47	L2
L1	OX-2 or MRC-OX-2 or CD200 or MOX1 or OX-2R	119	L1

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NCBI PubMed National Library of Medicine NLM

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

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Related Resources

1: Gorczynski RM, Hu J, Chen Z, Kai Y, Lei J. Related Articles, Links
A CD200FC immunoadhesin prolongs rat islet xenograft survival in mice.
Transplantation. 2002 Jun 27;73(12):1948-53.
PMID: 12131694 [PubMed - indexed for MEDLINE]

2: Gorczynski RM, Chen Z, Yu K, Hu J. Related Articles, Links
CD200 immunoadhesin suppresses collagen-induced arthritis in mice.
Clin Immunol. 2001 Dec;101(3):328-34.
PMID: 11726225 [PubMed - indexed for MEDLINE]

3: Gorczynski RM. Related Articles, Links
Evidence for an immunoregulatory role of OX2 with its counter ligand (OX2L) in the regulation of transplant rejection, fetal loss, autoimmunity and tumor growth.
Arch Immunol Ther Exp (Warsz). 2001;49(4):303-9. Review.
PMID: 11726033 [PubMed - indexed for MEDLINE]

4: Gorczynski RM, Chen Z, Hu J, Kai Y, Lei J. Related Articles, Links
Evidence of a role for CD200 in regulation of immune rejection of leukaemic tumour cells in C57BL/6 mice.
Clin Exp Immunol. 2001 Nov;126(2):220-9.
PMID: 11703364 [PubMed - indexed for MEDLINE]

5: Clark DA, Yu G, Levy GA, Gorczynski RM. Related Articles, Links
Procoagulants in fetus rejection: the role of the OX-2 (CD200) tolerance signal.
Semin Immunol. 2001 Aug;13(4):255-63. Review.
PMID: 11437633 [PubMed - indexed for MEDLINE]

6: Gorczynski RM, Chen Z, Lee L, Yu K, Hu J. Related Articles, Links
Anti-CD200R ameliorates collagen-induced arthritis in mice.
Clin Immunol. 2002 Sep;104(3):256-64.
PMID: 12217336 [PubMed - indexed for MEDLINE]

7: Nathan C, Muller WA. Related Articles, Links
Putting the brakes on innate immunity: a regulatory role for CD200?
Nat Immunol. 2001 Jan;2(1):17-9. No abstract available.
PMID: 11135572 [PubMed - indexed for MEDLINE]

☐ 8: Wright GJ, Jones M, Puklavec MJ, Brown MH, Barclay AN. Related Articles, Links

The unusual distribution of the neuronal/lymphoid cell surface CD200 (OX2) glycoprotein is conserved in humans.
Immunology. 2001 Feb;102(2):173-9.
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☐ 9: Dick AD, Broderick C, Forrester JV, Wright GJ. Related Articles, Links

Distribution of OX2 antigen and OX2 receptor within retina.
Invest Ophthalmol Vis Sci. 2001 Jan;42(1):170-6.
PMID: 11133863 [PubMed - indexed for MEDLINE]

☐ 10: Hoek RM, Ruuls SR, Murphy CA, Wright GJ, Goddard R, Zurawski SM, Blom B, Homola ME, Streit WJ, Brown MH, Barclay AN, Sedgwick JD. Related Articles, Links

Down-regulation of the macrophage lineage through interaction with OX2 (CD200).
Science. 2000 Dec 1;290(5497):1768-71.
PMID: 11099416 [PubMed - indexed for MEDLINE]

☐ 11: Gorczynski RM, Yu K, Clark D. Related Articles, Links

Receptor engagement on cells expressing a ligand for the tolerance-inducing molecule OX2 induces an immunoregulatory population that inhibits alloreactivity in vitro and in vivo.
J Immunol. 2000 Nov 1;165(9):4854-60.
PMID: 11046009 [PubMed - indexed for MEDLINE]

☐ 12: Gorczynski RM, Bransom J, Cattral M, Huang X, Lei J, Xiaorong L, Min WP, Wan Y, Gauldie J. Related Articles, Links

Synergy in induction of increased renal allograft survival after portal vein infusion of dendritic cells transduced to express TGFbeta and IL-10, along with administration of CHO cells expressing the regulatory molecule OX-2.
Clin Immunol. 2000 Jun;95(3):182-9.
PMID: 10866124 [PubMed - indexed for MEDLINE]

☐ 13: Ragheb R, Abrahams S, Beecroft R, Hu J, Ni J, Ramakrishna V, Yu G, Gorczynski RM. Related Articles, Links

Preparation and functional properties of monoclonal antibodies to human, mouse and rat OX-2.
Immunol Lett. 1999 Jun 1;68(2-3):311-5.
PMID: 10424437 [PubMed - indexed for MEDLINE]

☐ 14: Gorczynski RM, Cattral MS, Chen Z, Hu J, Lei J, Min WP, Yu G, Ni J. Related Articles, Links

An immunoadhesin incorporating the molecule OX-2 is a potent immunosuppressant that prolongs allo- and xenograft survival.
J Immunol. 1999 Aug 1;163(3):1654-60.
PMID: 10415071 [PubMed - indexed for MEDLINE]

☐ 15: Gorczynski RM, Cohen Z, Fu XM, Lei J. Related Articles, Links

Anti-rat OX-2 blocks increased small intestinal transplant survival after portal vein immunization.
Transplant Proc. 1999 Feb-Mar;31(1-2):577-8. No abstract available.
PMID: 10083244 [PubMed - indexed for MEDLINE]

☐16: Gorczynski L, Chen Z, Hu J, Kai Y, Lei J, Ramakrishna V, Gorczynski RM. Related Articles, Links

Evidence that an OX-2-positive cell can inhibit the stimulation of type 1 cytokine production by bone marrow-derived B7-1 (and B7-2)-positive dendritic cells.
J Immunol. 1999 Jan 15;162(2):774-81.
PMID: 9916698 [PubMed - indexed for MEDLINE]

☐17: Gorczynski RM, Chen Z, Fu XM, Zeng H. Related Articles, Links

Increased expression of the novel molecule OX-2 is involved in prolongation of murine renal allograft survival.
Transplantation. 1998 Apr 27;65(8):1106-14.
PMID: 9583873 [PubMed - indexed for MEDLINE]

☐18: Chen Z, Zeng H, Gorczynski RM. Related Articles, Links

Cloning and characterization of the murine homologue of the rat/human MRC OX-2 gene.
Biochim Biophys Acta. 1997 Nov 28;1362(1):6-10.
PMID: 9434094 [PubMed - indexed for MEDLINE]

☐19: Preston S, Wright GJ, Starr K, Barclay AN, Brown MH. Related Articles, Links

The leukocyte/neuron cell surface antigen OX2 binds to a ligand on macrophages.
Eur J Immunol. 1997 Aug;27(8):1911-8.
PMID: 9295026 [PubMed - indexed for MEDLINE]

☐20: Borriello F, Lederer J, Scott S, Sharpe AH. Related Articles, Links

MRC OX-2 defines a novel T cell costimulatory pathway.
J Immunol. 1997 May 15;158(10):4548-54.
PMID: 9144466 [PubMed - indexed for MEDLINE]

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21: McCaughan GW, Clark MJ, Barclay AN. Related Articles, Links

Characterization of the human homolog of the rat MRC OX-2 membrane glycoprotein.

Immunogenetics. 1987;25(5):329-35.

PMID: 3032785 [PubMed - indexed for MEDLINE]

PubMed Services

22: Gorczynski RM. Related Articles, Links

Transplant tolerance modifying antibody to CD200 receptor, but not CD200, alters cytokine production profile from stimulated macrophages.

Eur J Immunol. 2001 Aug;31(8):2331-7.

PMID: 11477545 [PubMed - indexed for MEDLINE]

Related Resources

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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:05:32 ON 10 JAN 2003

L1	1317	S OX-2 OR MRC-OX-2 OR CD200 OR OX-2R OR OX2
L2	940	DUP REM L1 (377 DUPLICATES REMOVED)
L3	95	S L2 AND (DENDRITIC OR MACROPHAGE OR LYMPHOCYTE OR MONOCYTE)
L4	64	S L3 AND PY>1994

L4 ANSWER 1 OF 64 MEDLINE
ACCESSION NUMBER: 2002653670 MEDLINE
DOCUMENT NUMBER: 22300967 PubMed ID: 12414514
TITLE: Constitutive retinal **CD200** expression regulates resident microglia and activation state of inflammatory cells during experimental autoimmune uveoretinitis.
AUTHOR: Broderick Cathryn; Hoek Robert M; Forrester John V; Liversidge Janet; Sedgwick Jonathon D; Dick Andrew D
CORPORATE SOURCE: Department of Ophthalmology, University of Aberdeen, United Kingdom.
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, **(2002 Nov)** 161 (5) 1669-77.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20021105
Last Updated on STN: 20021211
Entered Medline: 20021122

AB Recent evidence supports the notion that tissue **OX2** (**CD200**) constitutively provides down-regulatory signals to myeloid-lineage cells via **CD200**-receptor (CD200R). Thus, mice lacking **CD200** (**CD200**(-/-)) show increased susceptibility to and accelerated onset of tissue-specific autoimmunity. In the retina there is extensive expression of **CD200** on neurons and retinal vascular endothelium. We show here that retinal microglia in **CD200**(-/-) mice display normal morphology, but unlike microglia from wild-type **CD200**(+/+) mice are present in increased numbers and most significantly, express inducible nitric oxide synthase (NOS2), a **macrophage** activation marker. Onset and severity of uveitogenic peptide (1-20) of interphotoreceptor retinoid-binding protein-induced experimental autoimmune uveoretinitis is accelerated in **CD200** (-/-) mice and although tissue destruction appears no greater than seen in **CD200**(+/+) mice, there is continued increased ganglion and photoreceptor cell apoptosis. Myeloid cell infiltrate was increased in **CD200**(-/-) mice during experimental autoimmune uveoretinitis, although NOS2 expression was not heightened. The results indicate that the **CD200**:CD200R axis regulates retinal microglial activation. In **CD200**(-/-) mice the release of suppression of tonic **macrophage** activation, supported by increased NOS2 expression in the **CD200**(-/-) steady state accelerates disease onset but without any demonstration of increased target organ/tissue destruction.

L4 ANSWER 2 OF 64 MEDLINE
ACCESSION NUMBER: 2002627387 MEDLINE
DOCUMENT NUMBER: 22206107 PubMed ID: 12217336
TITLE: Anti-CD200R ameliorates collagen-induced arthritis in mice.
AUTHOR: Gorczynski Reginald M; Chen Zhiqi; Lee Lydia; Yu Kai; Hu Jiang
CORPORATE SOURCE: Transplant Research Division, The Toronto Hospital, 200 Elizabeth Street, Toronto, Ontario, M5G2C4, Canada.
SOURCE: CLINICAL IMMUNOLOGY, **(2002 Sep)** 104 (3) 256-64.
Journal code: 100883537. ISSN: 1521-6616.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20021019
Last Updated on STN: 20021213
Entered Medline: 20021104

AB Immunization of DBA/1 with 100 microg bovine collagen type II emulsified in Freund's adjuvant, followed by booster injection in incomplete adjuvant at 18 days, leads to development of arthritis in more than 70% of mice by 28 days postinjection. We have previously shown that the novel immunosuppressant molecule CD200Fc (linking an extracellular domain of **CD200** with a murine IgG2a Fc region) can suppress induction of disease when given to mice from the time of collagen injection. This occurs in concert with a decrease in the serum levels of anti-collagen IgG (approximately 50% reduction), with relatively more IgG2b and IgG3, decreased serum levels of TNFalpha and IFN-gamma, and decreased production of those same cytokines after restimulation of **lymphocytes** in vitro with collagen. Since **CD200** induces suppression following engagement of a receptor (CD200R), known to be expressed on, among other cells, **macrophages**, we investigated whether infusion of anti-CD200R and/or CD200Fc would ameliorate established disease in DBA mice, when injections were begun following collagen immunization. Our data indicate an arrest of disease following either treatment, with modification of a number of immune parameters (serum and **lymphocyte** cytokine production) consistent with a general role for **CD200**:CD200R interactions in the regulation of induction and/or expression of autoimmune disorders. When a higher dose (250 microg/mouse) of anti-CD200R was infused into a group of overtly arthritic mice, a significant (approximately 50%) decrease in arthritic joint score occurred over the 4-week treatment period.

L4 ANSWER 3 OF 64 MEDLINE
ACCESSION NUMBER: 2002487254 IN-PROCESS
DOCUMENT NUMBER: 22234700 PubMed ID: 12322892
TITLE: The same immunoregulatory molecules contribute to successful pregnancy and transplantation.
AUTHOR: Gorczynski Reginald M; Hadidi Sima; Yu Gary; Clark David A
CORPORATE SOURCE: Transplant Research Division, The Toronto Hospital, Ontario, Canada.. rgorczynski@uhnres.utoronto.ca
SOURCE: AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, **(2002 Jul)** 48 (1) 18-26.
Journal code: 8912860. ISSN: 1046-7408.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020927
Last Updated on STN: 20021213

AB PROBLEM: At least two **dendritic** cell-associated molecules have been shown to contribute to the successful outcome of organ and tissue allografts in mice, namely **CD200** and MD-1. **CD200** is up-regulated in rodent transplantation models where successful inhibition of rejection is accomplished, and is believed to signal immunosuppression following engagement of a receptor, CD200R, on **macrophages** and/or gammadelta T-cell receptor (gammadelta TCR+ cells MD-1 is

implicated in controlling expression of costimulatory molecules including CD80/CD86 which induce an immunorejection response, and thus inhibition of

MD-1 expression also facilitates increased graft survival MD-1 also stabilizes expression of CD14, part of the receptor complex for LPS. As well as the inhibition of rejection which follows blockade of MD-1 expression and/or augmentation of **CD200** expression, an altered polarization in cytokine production is seen, with increased expression of interleukin-4 (IL-4), IL-10 and transforming growth factor-beta (TGF-beta), and decreased IL-2, interferon-gamma (IFN-gamma) and tumor nerosis factor-alpha (TNF-alpha). Successful pregnancy in allopregnant mice also depends upon control of graft rejection mechanisms. Proinflammatory T-helper 1 (Th1) cytokines (TNF-alpha + IFN-gamma + IL-1) have been shown to cause spontaneous abortion in mice by activating a novel prothrombinase, fibrinogen-like peptide (fibroleukin) fgl2, which may promote fibrin deposition in the graft rejection process; expression of IL-10, TGF-beta, and progesterone-induced blocking factor (PIBF) in contrast leads to lowering of abortion rates. Interestingly, the spontaneous abortion rates in abortion-prone CBA x DBA/2 matings and in the low abortion rate CBA x BALB/c matings were lower than the frequency of implantation sites showing fibrin(hi) + fgl2 (mRNA)hi, implying regulation of the pro-abortion consequences of fgl2 expression. METHODS: We have investigated, by in situ hybridization, **CD200**, MD-1 and fgl2 expression in implantation sites in different strains of mice, and studied the effects of anti-MD-1, anti-**CD200** and CD200Fc immunoadhesin on fetal and allograft survival. The role of indoleamine dioxygenase (IDO) was evaluated. RESULTS: **CD200** mRNA expression occurred in the same sites as fgl2 mRNA. Anti-**CD200** antibody raised the abortion rate to predicted levels, and infusion of a **CD200** immunoadhesin reduced the abortion rate, as did an anti-MD-1 antibody. The latter also improved organ and tissue graft survival. Suppression by antigen-presenting **macrophages** triggered by **CD200** is dependent upon intact IDO activity. CONCLUSION: Regulation of **CD200** and MD-1 expression may control both pregnancy and allograft survival.

L4 ANSWER 4 OF 64 MEDLINE
ACCESSION NUMBER: 2002383669 MEDLINE
DOCUMENT NUMBER: 22127239 PubMed ID: 12131694
TITLE: A CD200FC immunoadhesin prolongs rat islet xenograft survival in mice.
AUTHOR: Gorczynski R M; Hu J; Chen Z; Kai Y; Lei J
CORPORATE SOURCE: The Toronto Hospital, University Health Network and Department of Surgery, University of Toronto, Toronto, Canada M5G2C4.
SOURCE: TRANSPLANTATION, **(2002 Jun 27)** 73 (12) 1948-53. Journal code: 0132144. ISSN: 0041-1337.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020723
Last Updated on STN: 20020801
Entered Medline: 20020731

AB BACKGROUND: A solubilized form of the **CD200** molecule, CD200Fc, has been shown to suppress allograft rejection and development of collagen-induced arthritis in mice. We investigated whether the same molecule could prolong survival of rat islet xenografts. METHODS: Streptozocin-treated mice, receiving injections with anti-asialo-GM1

antibody, received rat islets (approximately 400/mouse) under the kidney capsule or injected into the portal vein, along with rapamycin treatment. Thereafter mice received injections of CD200Fc (10 microg/mouse/injection) or control mouse IgG2. Blood glucose was monitored daily. Some mice received additional injections of anti-**CD200**/-CD200R monoclonal antibodies. RESULTS: Portal vein delivery of islets led to more extended resolution of diabetes than did transplantation under the kidney capsule. CD200Fc further prolonged survival in either case, an effect abolished by anti-**CD200** or F(ab')2 anti-CD200R mAbs, but not by whole anti-CD200R (anti-CD200R Ig). Spleen cells taken from CD200Fc-treated mice showed polarization to type-2 cytokine production (interleukin-4, interleukin-10) on restimulation with rat splenocytes in culture, in comparison to cells from control mice (type-1 cytokines, interlulin-2, interferon-gamma). CONCLUSION: **CD200**:CD200R interactions are important in regulating rat islet xenograft survival.

L4 ANSWER 5 OF 64 MEDLINE
ACCESSION NUMBER: 2002328639 MEDLINE
DOCUMENT NUMBER: 22068374 PubMed ID: 12072366
TITLE: **CD200** and membrane protein interactions in the control of myeloid cells.
AUTHOR: Barclay A Neil; Wright Gavin J; Brooke Gary; Brown Marion H
CORPORATE SOURCE: Sir William Dunn School of Pathology, University of Oxford, OX1 3RE, Oxford, UK.. barclay@molbiol.ox.ac.uk
SOURCE: Trends Immunol, **(2002 Jun)** 23 (6) 285-90. Ref: 59
Journal code: 100966032. ISSN: 1471-4906.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020620
Last Updated on STN: 20020820
Entered Medline: 20020819
AB **OX2** (now designated **CD200**) is a membrane protein expressed by a broad range of cell types. It is the ligand for a receptor restricted to myeloid cells, with the potential to deliver inhibitory signals. This is indicated by the **CD200**-deficient mouse model, in which myeloid cells are more activated when stimulated immunologically than cells from normal mice. The unusual tissue distribution of **CD200** indicates where myeloid cells can be restrictively controlled through cell-cell contact. Recent data on **CD200** will be reviewed in the context of other proteins that might have similar roles, in particular, the interaction between CD47 and SIRPalpha (CD172a).

L4 ANSWER 8 OF 64 MEDLINE
ACCESSION NUMBER: 2002046490 MEDLINE
DOCUMENT NUMBER: 21583292 PubMed ID: 11726225
TITLE: **CD200** immunoadhesin suppresses collagen-induced arthritis in mice.
AUTHOR: Gorczynski R M; Chen Z; Yu K; Hu J
CORPORATE SOURCE: Transplant Research Division, The Toronto Hospital, 200

Elizabeth Street, Toronto, Ontario, M5G2C4, Canada.
SOURCE: CLINICAL IMMUNOLOGY, **(2001 Dec)** 101 (3) 328-34.
Journal code: 100883537. ISSN: 1521-6616.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020124
Last Updated on STN: 20020125
Entered Medline: 20020110

AB DBA/1 mice immunized with 100 microg bovine collagen type II emulsified in Freund's adjuvant, followed by booster injection in incomplete adjuvant at 18 days, develop profound arthritis (>50% of animals) by 30 days postinjection. The molecule **CD200** (previously called **OX2**), associated with, among others, follicular **dendritic** cells, is implicated in delivery of immunosuppressive signals to the immune system, and an immunoadhesin in which the extracellular domains of **CD200** were linked to a mouse IgG2a Fc region has been shown to promote renal allograft survival. DBA/1 mice receiving 15 microg/mouse CD200Fc at 3-day intervals following immunization with collagen did not develop arthritis in this model. **Lymphocytes** taken from CD200Fc-treated, collagen-immunized mice produced significantly lower levels of TNFalpha and IFN-gamma in culture supernatants after restimulation in vitro with collagen, in contrast to cells taken from control mice treated with PBS or normal mouse Ig. Serum from CD200Fc-treated mice contained less anti-collagen IgG (approximately 50% reduction), with relatively more IgG2b and IgG3, and lower levels of TNFalpha and IFN-gamma, than control mice. These data indicate that this immunoadhesin may have a potent role to play in the regulation of autoimmune disorders.

L4 ANSWER 9 OF 64 MEDLINE
ACCESSION NUMBER: 2001679815 MEDLINE
DOCUMENT NUMBER: 21582469 PubMed ID: 11726033
TITLE: Evidence for an immunoregulatory role of **OX2** with its counter ligand (OX2L) in the regulation of transplant rejection, fetal loss, autoimmunity and tumor growth.
AUTHOR: Gorczynski R M
CORPORATE SOURCE: The Toronto Hospital, University Health Network, Ontario, Canada.. rgorczynski@transplantunit.org
SOURCE: ARCHIVUM IMMUNOLOGIAE ET THERAPIAE EXPERIMENTALIS, **(2001)** 49 (4) 303-9. Ref: 63
Journal code: 0114365. ISSN: 0004-069X.
PUB. COUNTRY: Poland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20011203
Last Updated on STN: 20020529
Entered Medline: 20020528

AB Transplantation has emerged as an effective treatment for patients with end-stage organ failure. Current regimens of non-specific immunosuppressive drug treatment, which are needed life-long to prevent

graft rejection, have numerous adverse side effects and increase the risk of opportunistic infections and malignancy. A major goal is to develop immunotherapeutic protocols that achieve specific tolerance. Such protocols would decrease and eventually eliminate the reliance on non-specific drug therapy. We showed that portal vein delivery of donor antigen prolongs the survival of vascularized and non-vascularized allo- and xeno-grafts, and that increased graft survival is associated with altered cytokine production and augmented expression of the molecule **OX2**. This review documents further evidence for a more general immunoregulatory role for the interactions of **OX2** and its ligand, OX2L.

L4 ANSWER 10 OF 64 MEDLINE
ACCESSION NUMBER: 2001650119 MEDLINE
DOCUMENT NUMBER: 21560360 PubMed ID: 11703364
TITLE: Evidence of a role for **CD200** in regulation of immune rejection of leukaemic tumour cells in C57BL/6 mice.
AUTHOR: Gorczynski R M; Chen Z; Hu J; Kai Y; Lei J
CORPORATE SOURCE: Department of Surgery and Immunology, University of Toronto, Toronto, Canada.. rgorczynski@transplantunit.org
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, **(2001 Nov)** 126 (2) 220-9.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011113
Last Updated on STN: 20020123
Entered Medline: 20011207
AB Increased expression of the molecule **CD200** in mice receiving renal allografts is associated with immunosuppression leading to increased graft survival, and altered cytokine production in **lymphocytes** harvested from the transplanted animals. Preferential production of IL-4, IL-10 and TGFbeta occurs on donor-specific restimulation in vitro, with decreased production of IL-2, IFNgamma and TNFalpha. These effects are enhanced by simultaneous infusion of **CD200** immunoadhesin (CD200Fc) and donor **CD200** receptor (CD200r) bearing **macrophages** to transplanted mice. C57BL/6 mice do not normally resist growth of EL4 or C1498 leukaemia tumour cells. Following transplantation of cyclophosphamide-treated C57BL/6 with T-depleted C3H bone marrow cells, or for the EL4 tumour, immunization of C57BL/6 mice with tumour cells transfected with a vector encoding the co-stimulatory molecule CD80 (EL4-CD80), mice resist growth of tumour challenge. Immunization of C57BL/6 mice with EL4 cells overexpressing CD86 (EL4-CD86) is ineffective. Protection from tumour growth in either model is suppressed by infusion of CD200Fc, an effect enhanced by co-infusion of CD200r+ **macrophages**. CD200Fc acts on both CD4+ and CD8+ cells to produce this suppression. These data are consistent with the hypothesis that immunosuppression following **CD200**-CD200r interaction can regulate a functionally important tumour growth inhibition response in mice.

L4 ANSWER 12 OF 64 MEDLINE
ACCESSION NUMBER: 2001429379 MEDLINE
DOCUMENT NUMBER: 21369585 PubMed ID: 11477545

TITLE: Transplant tolerance modifying antibody to **CD200** receptor, but not **CD200**, alters cytokine production profile from stimulated **macrophages**.
AUTHOR: Gorczynski R M
CORPORATE SOURCE: CCRW 2-855, The Toronto Hospital, University Health Network, Toronto, Ontario, Canada.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, **(2001 Aug)** 31 (8) 2331-7.
Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010917
Last Updated on STN: 20010917
Entered Medline: 20010913

AB Increased C57BL/6 allograft survival following donor-specific **dendritic** cell (DC) portal vein (pv) pre-transplant immunization of C3H mice is associated with increased expression of the molecule **CD200** on DC, delivery of suppressive signals by **CD200** (r+) **macrophages**, and polarization in cytokine production towards type-2 cytokines. Infusion of anti-mouse **CD200** monoclonal antibody abolishes these effects. We have used whole Ig, and F(ab')(2) fragments, of anti-**CD200** and anti-**CD200**(r) mAb to explore the relative signaling role of **CD200**(+) versus **CD200**(r+) cells in suppression of type-1 cytokine production in mixed leukocyte cultures (MLC), and enhanced graft survival in vivo. Simple neutralization of **CD200** [even by F(ab')(2) antibody] reversed **CD200**-mediated suppression. However, only whole anti-**CD200**(r) antibody was effective in stimulating suppression from **CD200**(r+) cells. Suppression of cytokine induction following cross-linking of **CD200**(r+) cells in vitro was attenuated by anti-IL-6 mAb. Our data are consistent with the hypothesis that **CD200**(r) itself delivers the crucial intracellular signal leading to immunosuppression, a feature likely of importance in autoimmunity and transplantation.

L4 ANSWER 15 OF 64 MEDLINE
ACCESSION NUMBER: 2001175102 MEDLINE
DOCUMENT NUMBER: 21170160 PubMed ID: 11135572
TITLE: Putting the brakes on innate immunity: a regulatory role for **CD200**?.
AUTHOR: Nathan C; Muller W A
SOURCE: Nat Immunol, **(2001 Jan)** 2 (1) 17-9.
Journal code: 100941354. ISSN: 1529-2908.
PUB. COUNTRY: United States
DOCUMENT TYPE: News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010417
Last Updated on STN: 20010417
Entered Medline: 20010412

L4 ANSWER 16 OF 64 MEDLINE
ACCESSION NUMBER: 2001168977 MEDLINE
DOCUMENT NUMBER: 21168966 PubMed ID: 11267422
TITLE: **Dendritic** cells expressing TGFbeta/IL-10, and CHO cells with **OX-2**, increase graft

survival.
AUTHOR: Gorczynski R; Bransom J; Cattral M; Huang X; Lei J; Min W; Wan Y; Gauldie J
CORPORATE SOURCE: University Health Network, Toronto, ON, Canada.
SOURCE: TRANSPLANTATION PROCEEDINGS, **(2001 Feb-Mar)** 33 (1-2) 1565-6.
Journal code: 0243532. ISSN: 0041-1345.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

L4 ANSWER 17 OF 64 MEDLINE
ACCESSION NUMBER: 2001064470 MEDLINE
DOCUMENT NUMBER: 20553647 PubMed ID: 11099416
TITLE: Down-regulation of the **macrophage** lineage through interaction with **OX2** (**CD200**).
AUTHOR: Hoek R M; Ruuls S R; Murphy C A; Wright G J; Goddard R; Zurawski S M; Blom B; Homola M E; Streit W J; Brown M H; Barclay A N; Sedgwick J D
CORPORATE SOURCE: DNAX Research Institute of Molecular and Cellular Biology, 901 California Avenue, Palo Alto, CA 94304, USA.
SOURCE: SCIENCE, **(2000 Dec 1)** 290 (5497) 1768-71.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222
AB **OX2** (**CD200**) is a broadly expressed membrane glycoprotein, shown here to be important for regulation of the **macrophage** lineage. In mice lacking **CD200**, **macrophage** lineage cells, including brain microglia, exhibited an activated phenotype and were more numerous. Upon facial nerve transection, damaged **CD200**-deficient neurons elicited an accelerated microglial response. Lack of **CD200** resulted in a more rapid onset of experimental autoimmune encephalomyelitis (EAE). Outside the brain, disruption of **CD200**-**CD200** receptor interaction precipitated susceptibility to collagen-induced arthritis (CIA) in mice normally resistant to this disease. Thus, in diverse tissues **OX2** delivers an inhibitory signal for the **macrophage** lineage.

L4 ANSWER 18 OF 64 MEDLINE
ACCESSION NUMBER: 2001033110 MEDLINE
DOCUMENT NUMBER: 20501084 PubMed ID: 11046009
TITLE: Receptor engagement on cells expressing a ligand for the tolerance-inducing molecule **OX2** induces an immunoregulatory population that inhibits alloreactivity in vitro and in vivo.
AUTHOR: Gorczynski R M; Yu K; Clark D
CORPORATE SOURCE: University Health Network, Toronto, Canada.

SOURCE: JOURNAL OF IMMUNOLOGY, **(2000 Nov 1)** 165 (9) 4854-60.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001130

AB Increased survival of C57BL/6 renal allografts following portal vein donor-specific pretransplant immunization of C3H mice is associated with increased expression of the molecule **OX2** seen on host **dendritic** cells, along with a marked polarization in cytokine production from **lymphocytes** harvested from the transplanted animals, with preferential production of IL-4, IL-10, and TGF-beta on donor-specific restimulation in vitro, and decreased production of IL-2, IFN-gamma, and TNF-alpha compared with non-portal vein-immunized control transplanted mice. The increased renal allograft survival and the altered cytokine production are abolished by infusion of anti-mouse **OX2** mAb (3B6). Infusion of a soluble **OX2**:Fc immunoadhesin can itself produce significant prolongation of xeno- and allografts in mice. We have used FITC-conjugated **OX2**:Fc to characterize cells expressing a ligand (OX2L) for **OX2**, and provide evidence that subpopulations of LPS-stimulated splenic **macrophages**, Con A-activated splenic T cells, and the majority (>80%) of gammadeltaTCR(+) T cells express this ligand. We show below that F4/80(+), OX2L(+) splenic **macrophages** , admixed with **OX2**:Fc, represent a potent immunosuppressive population capable of causing more profound inhibition of alloreactivity in vitro or in vivo than that seen using either **OX2**:Fc or **OX2**(+) (or OX2L(+)) cells alone. Immunoregulation by this OX2L(+) population occurs in an MHC-restricted fashion.

L4 ANSWER 20 OF 64 MEDLINE
ACCESSION NUMBER: 2000455726 MEDLINE
DOCUMENT NUMBER: 20434845 PubMed ID: 10981966
TITLE: Lymphoid/neuronal cell surface **OX2** glycoprotein recognizes a novel receptor on **macrophages** implicated in the control of their function.
AUTHOR: Wright G J; Puklavec M J; Willis A C; Hoek R M; Sedgwick J D; Brown M H; Barclay A N
CORPORATE SOURCE: Sir William Dunn School of Pathology, University of Oxford, United Kingdom.
SOURCE: IMMUNITY, **(2000 Aug)** 13 (2) 233-42.
Journal code: 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF231392; GENBANK-AF231393
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000925

AB The **OX2** membrane glycoprotein (**CD200**) is expressed on a broad range of tissues including lymphoid cells, neurons, and endothelium. We report the characterization of an **OX2** receptor (OX2R) that is a novel protein restricted to cells of the myeloid lineage.

OX2 and its receptor are both cell surface glycoproteins containing two immunoglobulin-like domains and interact with a dissociation constant of 2.5 microM and koff 0.8 s(-1), typical of many leukocyte protein membrane interactions. Pervanandate treatment of **macrophages** showed that OX2R could be phosphorylated on tyrosine residues. Blockade of the **OX2**-OX2R interaction with an OX2R mAb exacerbated the disease model experimental allergic encephalomyelitis. These data, together with data from an **OX2**-deficient mouse (R. M. Hoek et al., submitted), suggest that myeloid function can be controlled in a tissue-specific manner by the **OX2**-OX2R interaction.

L4 ANSWER 24 OF 64 MEDLINE
ACCESSION NUMBER: 1999351723 MEDLINE
DOCUMENT NUMBER: 99351723 PubMed ID: 10424437
TITLE: Preparation and functional properties of monoclonal antibodies to human, mouse and rat **OX-2**
.
AUTHOR: Ragheb R; Abrahams S; Beecroft R; Hu J; Ni J; Ramakrishna V; Yu G; Gorczynski R M
CORPORATE SOURCE: Transplant Research Division, The Toronto Hospital, ON, Canada.
SOURCE: IMMUNOLOGY LETTERS, **(1999 Jun 1)** 68 (2-3) 311-5.
Journal code: 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990916

AB We have prepared mouse and rat hybridomas to a 43-kDa molecule expressed in the thymus, on a subpopulation of **dendritic** cells, and in the brain, in mammalian tissue derived from mouse, rat and human. Using CHO cells transiently transfected with adenovirus vector(s) expressing a cDNA construct for the relevant **OX-2** gene, we show these monoclonal antibodies (Mabs) detect a molecule encoded by this construct (rat **OX-2** (rOX-2), mouse **OX-2** (mOX-2) and human **OX-2** (huOX-2), respectively). Furthermore, at least some of the anti-rat Mabs detect determinants expressed on the murine **OX-2** molecule, as we predicted in an earlier publication. Previous studies have implied that this molecule might serve an important role in regulation of cell signaling for cytokine production. Using one-way mixed leukocyte reactions we show that when cells are cultured in the presence of the species-specific Mab, cytokine production becomes polarized 'away from' type-2 cytokine production, with preferentially increased expression of type-1 cytokine production.

L4 ANSWER 25 OF 64 MEDLINE
ACCESSION NUMBER: 1999343781 MEDLINE
DOCUMENT NUMBER: 99343781 PubMed ID: 10415071
TITLE: An immunoadhesin incorporating the molecule **OX-2** is a potent immunosuppressant that prolongs allo- and xenograft survival.
AUTHOR: Gorczynski R M; Cattral M S; Chen Z; Hu J; Lei J; Min W P; Yu G; Ni J
CORPORATE SOURCE: Transplant Research Division, The Toronto Hospital,

Canada.. rgorczynski@transplantunit.org
SOURCE: JOURNAL OF IMMUNOLOGY, **(1999 Aug 1)** 163 (3) 1654-60.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990820
Last Updated on STN: 19990820
Entered Medline: 19990812

AB We have established that, in mice receiving donor-specific immunization by the portal vein, the increased graft survival seen is associated with the increased expression of a molecule (**OX-2**) on a subpopulation of **dendritic** cells (DC), and polarization of cytokine production to type 2 cytokines on Ag-specific restimulation of cells from these mice. Furthermore, infusion of a mAb to **OX-2** blocks both the increased graft survival and the altered cytokine production seen. We have constructed an immunoadhesin in which the extracellular domain of **OX-2** is linked to the murine IgG2a Fc region, and we have expressed this molecule (**OX-2**:Fc) in a eukaryotic (baculovirus) expression system. Incubation of **lymphocytes** with 50 ng/ml **OX-2**:Fc inhibits a primary mixed **lymphocyte** reaction in vitro, as assayed by proliferation and induction of cytotoxic T cells, and also alters cytokine production with decreased IL-2 (IFN-gamma) production and increased IL-4 (IL-10) production. Similarly, in vivo infusion of **OX-2**:Fc promotes increased allo- and xenograft (both skin and renal grafts) survival and decreases the Ab response to sheep erythrocytes. Our data suggest this molecule might have clinical importance in allo- and xenotransplantation.

L4 ANSWER 26 OF 64 MEDLINE
ACCESSION NUMBER: 1999113736 MEDLINE
DOCUMENT NUMBER: 99113736 PubMed ID: 9916698
TITLE: Evidence that an **OX-2**-positive cell can inhibit the stimulation of type 1 cytokine production by bone marrow-derived B7-1 (and B7-2)-positive **dendritic** cells.
AUTHOR: Gorczynski L; Chen Z; Hu J; Kai Y; Lei J; Ramakrishna V; Gorczynski R M
CORPORATE SOURCE: Transplant Research Division, Toronto Hospital, Ontario, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, **(1999 Jan 15)** 162 (2) 774-81.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 19990223
Entered Medline: 19990208

AB We reported that hepatic mononuclear, nonparenchymal cells (NPC) can inhibit the immune response seen when allogeneic C57BL/6 **dendritic** cells (DC) are incubated with C3H spleen responder cells. Cells derived from these cultures transfer increased survival of C57BL/6 renal allografts in C3H mice. We also found that increased expression of **OX-2** on DC was associated with inhibition of cytokine production and renal allograft rejection. We explored whether inhibition by hepatic NPC was a function of **OX-2** expression by these cells. Fresh C57BL/6 spleen-derived DC were cultured with C3H spleen responder cells and other putative coregulatory cells. The latter were derived from fresh C3H or C57BL/6 liver NPC, or from C3H or C57BL/6 mice treated for 10 days by i.v. infusion of human Flt3 ligand. Different populations of murine bone marrow-derived DC from cultures of bone marrow with IL-4 plus granulocyte-**macrophage**-CSF were also used as a source of putative regulator cells. Supernatants of all stimulated cultures were examined for functional expression of different cytokines (IL-2, IL-4, IFN-gamma, and TGFbeta). We found that fresh C57BL/6 splenic DC induced IL-2, not IL-4, production. Cells from the sources indicated inhibited IL-2 and IFN-gamma production and promoted IL-4 and TGFbeta production. Inhibition was associated with increased expression of **OX-2** on these cells, as defined by semiquantitative PCR and FACS analysis. By size fractionation, cells expressing **OX-2** were a subpopulation of NLDC145+ cells. Our data imply a role for cells expressing **OX-2** in the regulation of induction of cytokine production by conventional allostimulatory DC.

L4 ANSWER 32 OF 64 MEDLINE
ACCESSION NUMBER: 97289561 MEDLINE
DOCUMENT NUMBER: 97289561 PubMed ID: 9144466
TITLE: **MRC OX-2** defines a novel T cell costimulatory pathway.
AUTHOR: Borriello F; Lederer J; Scott S; Sharpe A H
CORPORATE SOURCE: Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA.. frank@mbcrr.harvard.edu
SOURCE: JOURNAL OF IMMUNOLOGY, **(1997 May 15)** 158 (10) 4548-54.

Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970602

AB T cell activation requires the engagement of the TCR as well as a second, costimulatory signal. In this study, we demonstrate that **MRC OX-2** (**OX-2**) mediates a previously unrecognized T cell costimulatory signal leading to enhanced T cell proliferation. One extensively studied costimulatory pathway, the B7/CD28 pathway, delivers its signal when CD28 is engaged by either of two ligands, B7-1 or B7-2, expressed on APC. Recent data have suggested that an additional ligand may exist in this pathway. This possibility prompted us to search previously cloned genes with both structural and expression characteristics similar to B7-1 and B7-2. Our search yielded **OX-2**, a rat **lymphocyte** activation marker, as a promising candidate gene. We now report that Chinese hamster ovary cell transfectants expressing the **OX-2** protein can costimulate murine CD4+ T cells to proliferate in an Ag-independent fashion using anti-CD3, as well as an Ag-dependent fashion using peptide. In contrast to B7-1-mediated costimulation, **OX-2** does not result in detectable levels of IL-2, IL-4, or IFN-gamma. In addition, **OX-2** transfectants do not bind the soluble receptor reagents of the B7/CD28 pathway (CD28-Ig and CTLA4Ig). Furthermore, **OX-2** costimulation is not inhibited by CTLA4Ig, as is B7-1-mediated costimulation, but is readily inhibited with an anti-**OX-2** mAb. Thus, **OX-2** is a T cell costimulatory ligand that acts through a non-B7/CD28 pathway, which leads to functionally distinct consequences, as reflected by the resulting cytokine profile.

L4 ANSWER 34 OF 64 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:906505 CAPLUS
DOCUMENT NUMBER: 138:12292
TITLE: Cloning and characterization of mouse **CD200** receptor variants, and therapeutic use thereof in modulating immune response in animal transplantation and immune diseases
INVENTOR(S): Gorczynski, Reginald M.; Marsden, Philip
PATENT ASSIGNEE(S): Transplantation Technologies Inc., Can.
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002095030	A2	20021128	WO 2002-CA734	20020524 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,

TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-292950P P 20010524
US 2002-369862P P 20020405

AB The present invention relates to **CD200** receptor isoforms and modulators thereof and their use in methods of immune modulation and pharmaceutical compns. In particular, protein and cDNA sequences for three isoforms of the murine **CD200** receptor called CD200R2a, CD200R2b and CD200R3a are provided. The inventors have also prepd. antibodies to the different isoforms of CD200R. Studies of using CD200R antibodies, co-administering the **CD200** receptor with a **CD200** peptide, preferably in the form of a sol. fusion protein, such as **CD200**:Fc, to modulate immune response are presented. The inventors have also shown that administering antibody fragments [e.g. Fab or F(ab')2 fragments] that bind to a **CD200** receptor inhibits the immune suppression caused by **CD200**. Accordingly, in another aspect, the present invention provides a method of inhibiting immune suppression by administering an effective amt. of a **CD200** receptor antagonist to a cell or animal in need thereof. Preferably, the antagonist is an agent that inhibits the interaction of the **CD200** receptor with **CD200**.

L4 ANSWER 35 OF 64 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:849661 CAPLUS
DOCUMENT NUMBER: 137:347560
TITLE: Protein and cDNA sequence of human and mouse cytokine **ox2** receptors
INVENTOR(S): Van der Vuurst de Vries, Anne-Renee; Galibert, Laurent J.
PATENT ASSIGNEE(S): Immunex Corporation, USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088164	A1	20021107	WO 2002-US13087	20020425 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-286686P P 20010426

AB The invention relates to protein and cDNA sequence of human and mouse cytokine **ox2** receptors. **Ox2** is a transmembrane protein, designated as human leukocyte antigen **CD200**. The receptors are also useful in screening for inhibitors or agonists thereof.
The invention further relates to prepn. of antibody for **ox2**

receptor.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 38 OF 64 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:122819 CAPLUS
DOCUMENT NUMBER: 136:177960
TITLE: Methods and compositions for modulating tumor growth by inhibiting **OX-2**
INVENTOR(S): Gorczynski, Reginald M.; Clark, David A.
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2002011762	A2	20020214	WO 2001-CA1111	20010730	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2001078338	A5	20020218	AU 2001-78338	20010730	<--

PRIORITY APPLN. INFO.: US 2000-222725P P 20000803
WO 2001-CA1111 W 20010730

AB Methods and compns. for regulating tumor growth are disclosed. For reducing tumor growth, agents that inhibit **OX-2** (**CD200**) are administered. Such methods are useful in treating cancer. For enhancing tumor growth, an **OX-2** protein or a nucleic acid encoding an **OX-2** protein is administered. Such methods are useful in studying cancer and/or tumor metastasis.

L4 ANSWER 40 OF 64 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:693368 CAPLUS
DOCUMENT NUMBER: 135:267229
TITLE: Methods and compositions for immunoregulation
INVENTOR(S): Gorczynski, Reginald M.; Clark, David A.
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2001068697	A2	20010920	WO 2001-CA346	20010316	<--
WO 2001068697	A3	20020510			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,					

CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1263786 A2 20021211 EP 2001-914889 20010316 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2000-189986P P 20000317
WO 2001-CA346 W 20010316

AB Methods and compns. for inducing immune suppression are disclosed. The methods involve administering an effective amt. of an agent that inhibits MD-1 with or without an **OX-2** protein or a nucleic acid encoding an **OX-2** protein. The methods are useful in preventing graft rejection, fetal loss, autoimmune disease, and allergies.
Methods and compns. for preventing immune suppression are also disclosed. The methods involve administering an effective amt. of MD-1 or an agent that activates or stimulates MD-1.

L4 ANSWER 41 OF 64 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:687850 CAPLUS
DOCUMENT NUMBER: 136:245923
TITLE: Does successful allopregnancy mimic transplantation tolerance?
AUTHOR(S): Gorczynski, Reginald M.; Yu, Gary; Clark, David A.
CORPORATE SOURCE: RM CCRW-2-855, Toronto Hospital, Toronto, ON, M5G2C4, Can.
SOURCE: Graft (Thousand Oaks, CA, United States) (**2001**), 4(5), 338-345
CODEN: GTOCA5; ISSN: 1522-1628
PUBLISHER: Sage Science Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The **dendritic**-cell assocd. mol. **CD200** is up-regulated in rodent transplantation models where successful inhibition of rejection is accomplished. The mechanism by which **CD200** achieves this effect involves signaling a receptor, CD200r, on **macrophages** and/or .gamma..delta.TCR+ cells, both of which have been implicated in adoptive transfer of tolerance. In addn. to inhibition of rejection, increased expression of **CD200** is assocd. with altered polarization in cytokine prodn., with increased expression of IL-4, IL-10 and TGF.beta., and decreased IL-2, IFN.gamma. and TNF-.alpha..
Inhibition of rejection can thus be adoptively transferred by IL-10/TGF.beta. and a **CD200** immunoadhesin and in turn can be inhibited by neutralizing these cytokines or by functional blockade of **CD200** expression. Successful pregnancy in allopregnant mice can also be viewed as dependent upon control of graft rejection. Proinflammatory Th1 cytokines (TNF-.alpha. + IFN-.gamma. + IL-1) can cause spontaneous abortion in mice by a mechanism which involves a novel prothrombinase, fgl2, which promotes fibrin deposition. However, we found that spontaneous abortion rates in abortion-prone CBA .times. DBA/2 matings and in low abortion rate CBA .times. BALB/c matings were lower

than the frequency of implantation sites showing fibrinhi + fgl2 mRNAhi. **CD200** expression was present in the same sites as fgl2 mRNA, and neutralization of this **CD200** expression by anti-**CD200** antibody raised the abortion rate to predicted levels. Conversely, a **CD200** immunoadhesin dramatically reduced the abortion rate. We hypothesize that in addn. to its role in organ and tissue allograft rejection, **CD200** expression is involved in the prevention of spontaneous abortion triggered by cytokine up-regulation of fgl2 at the feto-maternal interface.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 64 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:741947 CAPLUS
DOCUMENT NUMBER: 133:291146
TITLE: Novel uses of mammalian **OX2** protein and related reagents
INVENTOR(S): Hoek, Robert M.; Sedgwick, Jonathan D.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2000061171	A2	20001019	WO 2000-US9719	20000412	<--
WO 2000061171	A3	20010125			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
EP 1171154	A2	20020116	EP 2000-923257	20000412	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002541210	T2	20021203	JP 2000-610503	20000412	<--
US 2002192215	A1	20021219	US 2002-86972	20020301	<--

PRIORITY APPLN. INFO.:

US 1999-129124P	P	19990413
US 1999-290825	A	19990413
US 2000-547432	B3	20000412
WO 2000-US9719	W	20000412

AB Compns. and methods for using mammalian ligand **OX2** to treat an abnormal physiol. condition in an individual. The methods comprise administering a therapeutically effective amt. of **OX2** alone, or in combination with other therapeutic reagents; or an **OX2** antagonist.

L4 ANSWER 47 OF 64 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:511666 CAPLUS
DOCUMENT NUMBER: 127:120710
TITLE: T cell-mediated immune response modulation by **OX-2** costimulatory molecule and its

agonists and antagonists
INVENTOR(S): Borriello, Francescopaolo; Sharpe, Arlene H.
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721450	A1	19970619	WO 1996-US19189	19961127 <--

W: AU, CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9711440	A1	19970703	AU 1997-11440	19961127 <--

PRIORITY APPLN. INFO.: US 1995-8754P P 19951208
WO 1996-US19189 W 19961127

AB Methods and compns. for using the **OX-2** protein to modulate a T cell-mediated immune response are described. Novel structure forms of **OX-2** T cell costimulatory mols. are described. These structural forms comprise a novel structure domain or have a structural domain deleted. The structural forms correspond to naturally-occurring alternatively-spliced forms of **OX-2** T cell costimulatory mols. or variants thereof which can be produced by std. recombinant DNA techniques. The novel structure forms of the **OX-2** T cell costimulatory mols. can be used to identify agents which stimulate the expression of alternative forms of costimulatory mols. and to identify components of the signal transduction pathway which results in costimulation of T cells.

L4 ANSWER 48 OF 64 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999097997 EMBASE
TITLE: Anti-rat **OX-2** blocks increased small intestinal transplant survival after portal vein immunization.
AUTHOR: Gorczynski R.M.; Cohen Z.; Fu X.M.; Lei J.
CORPORATE SOURCE: Dr. R.M. Gorczynski, Toronto Hospital, Transplant Research CCRW-2-855, Toronto, Ont. M5G 2CH, Canada
SOURCE: Transplantation Proceedings, (1999) 31/1-2 (577).
Refs: 8
ISSN: 0041-1345 CODEN: TRPPA8
PUBLISHER IDENT.: S 0041-1345(98)01563-2
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
048 Gastroenterology
LANGUAGE: English

L4 ANSWER 51 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:370418 BIOSIS
DOCUMENT NUMBER: PREV200200370418
TITLE: Regulatory role of **CD200** on **dendritic** cells.
AUTHOR(S): Diao, Jun (1); Gorczynski, Reginald; Cattral, Mark (1)
CORPORATE SOURCE: (1) Surgery, University of Toronto, 200 Elizabeth St., Toronto, ON, M5G 2C4 Canada
SOURCE: FASEB Journal, (**March 22, 2002**) Vol. 16, No. 5,

pp. A1032. http://www.fasebj.org/. print.
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.

DOCUMENT TYPE: Conference
LANGUAGE: English

AB Regulatory role of **CD200** on **dendritic** cells **CD200**, formerly known as **OX-2**, is a glycoprotein expressed on a variety of lymphoid and neuronal cells and tissues; the expression of **CD200** receptor is limited to myeloid-derived cells, particularly **macrophages** and **dendritic** cells (DCs). Recent studies suggest that **CD200** might act as an inhibitor for myeloid activation, and play a role in autoimmunity and transplantation rejection. We investigated the effect of increased expression of **CD200** in mouse bone marrow-derived DCs. DCs were transduced with an adenovirus vector encoding the **CD200** gene (Ad5CD200). Transduction efficiency was vector-dose dependent; 70-80% DCs were transduced at a multiplicity of infection of 500, as judged by flow cytometry. Untransduced DCs expressed low levels of **CD200**. Exposure of DC to Ad5CD200 or control adenovirus vector (Ad5-ctr) was associated with increased expression of the costimulatory molecules CD40 and CD86, as compared to non-treated DCs. The expression of **CD200** remained stable following Ad5-ctr exposure. DCs expressing high levels of **CD200** had a significantly reduced stimulatory capacity in mixed allogeneic **lymphocyte** cultures, despite increased costimulatory molecule expression. Our data suggests that increased expression of **CD200** may promote the tolerogenic capacity of DCs.

L4 ANSWER 52 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:557960 BIOSIS
DOCUMENT NUMBER: PREV200100557960
TITLE: Role of **CD200**:CD200r interactions in regulating islet xenograft rejection.
AUTHOR(S): Gorczynski, R. (1); Hu, J. (1); Kai, Y. (1); Wong, A. (1); Lei, J. (1)
CORPORATE SOURCE: (1) Toronto Hospital, Toronto Canada
SOURCE: Xenotransplantation, (**August, 2001**) Vol. 8, No. Supplement 1, pp. 79. print.
Meeting Info.: VI Congress of the International Xenotransplantation Association Chicago, Illinois, USA September 29-October 03, 2001
ISSN: 0908-665X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 57 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:82960 BIOSIS
DOCUMENT NUMBER: PREV200100082960
TITLE: Viral homologues of cell surface proteins **OX2** and CD47 have potential to regulate **macrophage** function.
AUTHOR(S): Wright, G. J. (1); Vernon-Wilson, Elizabeth (1); Foster, Mildred (1); Brown, M. H. (1); Barclay, A. N. (1)
CORPORATE SOURCE: (1) Sir William Dunn School of Pathology, University of Oxford, Oxford, OX1 3RE UK
SOURCE: Immunology, (**December, 2000**) Vol. 101, No. Supplement 1, pp. 50. print.

Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 58 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:82882 BIOSIS
DOCUMENT NUMBER: PREV200100082882
TITLE: Interactions of cytoplasmic region of OX2R are consistent with an inhibitory function.
AUTHOR(S): Hutchings, N. J. (1); Brooke, G. (1); Chalkley, R.; Wright,
G. J. (1); Brown, M. H. (1); Barclay, A. N. (1)
CORPORATE SOURCE: (1) Sir William Dunn School of Pathology, University of Oxford, Oxford, OX1 3RE UK
SOURCE: Immunology, (**December, 2000**) Vol. 101, No. Supplement 1, pp. 24. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L4 ANSWER 63 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:164806 BIOSIS
DOCUMENT NUMBER: PREV199900164806
TITLE: The lymphoid/neuronal **OX2** antigen bind a novel **macrophage** cell surface protein.
AUTHOR(S): Wright, Gavin J.; Barclay, A. Neil; Brown, Marion H.
CORPORATE SOURCE: MRC CIU, Sir William Dunn Sch. Pathology, South Parks Road,
Oxford OX1 3RE UK
SOURCE: Immunology, (**Dec., 1998**) Vol. 95, No. SUPPL. 1, pp. 45.
Meeting Info.: 6th Annual Congress of the British Society for Immunology Harrogate, England, UK December 1-4, 1998
ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 64 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:102745 BIOSIS
DOCUMENT NUMBER: PREV199799401948
TITLE: Expression of a ligand for the immunoglobulin superfamily (IgSF) protein, MRC **OX2** in both the immune and nervous systems.
AUTHOR(S): Preston, Sandy; Brown, Marion H.; Barclay, A. Neil
CORPORATE SOURCE: MRC Cellular Immunology Unit, Sir William Dunn Sch. Pathol., Oxford OX1 3RE UK
SOURCE: Immunology, (1996) Vol. 89, No. SUPPL. 1, pp. 31.
Meeting Info.: Joint Congress of the British Society for Immunology and the Biochemical Society Harrogate, England, UK December 10-13, 1996
ISSN: 0019-2805.
DOCUMENT TYPE: Conference; Abstract; Conference

LANGUAGE: English